ARTICLE / INVESTIGACIÓN

Assessment of serum Pentraxin3 level in Iraq patients with and without Diabetic Retinopathy

Zena M Hassan[1], Rana A Hamdi[2], Khalaf G Hussein Al.Mohammadaw[3], Rassmia H Basal[4]
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[1] Basic Science, Department of Biochemistry, College of Medicine, University of Baghdad, Iraq.
[2] Clinical Biochemistry, Department of Biochemistry, College of Medicine, University of Baghdad, Iraq.
[3] Consultant physician Endocrinology Specialized Center for Endocrinology and Diabetes, Baghdad, Al-Rusafa, Iraq.
[4] M.B.C.HB. D.O.Internalmedicin, College of Medicine, University of Baghdad, Iraq.
Corresponding author: mzena4244@gmil.com

Abstract: Diabetic retinopathy is the main cause of vision loss worldwide. It is considered one of the most severe diabetic microvascular complications affecting the retina's blood vessels due to prolonged hyperglycemia. Pentraxin 3 is an acute-phase glycoprotein that is correlated with inflammation. Inflammation is mechanistically involved in the development of diabetic retinopathy. This study aims to measure serum pentraxin3 levels in type 2 diabetic patients with and without retinopathy and compare their levels to controls. Also, investigate the relationship between circulating pentraxin3 and the development of diabetic retinopathy. This case–control study included one hundred and twenty (120) individuals aged 40 to 70 years. Individuals were divided into 3 groups: Group 1 included 40 types 2 diabetic patients with retinopathy, group 2 included 40 type 2 diabetic patients without retinopathy and group 3- included 40 persons as controls. Significant increase in the mean value of serum pentraxin3 in the diabetic patient with retinopathy as compared to diabetic patients with and without retinopathy as compared to and control(p=0.000) as well as a significant increase in the mean value of serum pentraxin3 in the diabetic patient with retinopathy as compared to diabetic patients without retinopathy (p=0.000). In addition, a significant positive correlation was found between serum pentraxin3 level and HbA1C in diabetic patients with retinopathy group (r=0.936, p= 0.0001). Higher serum level of pentraxin 3 in diabetic patients with retinopathy and its association with poor glycemic control, as well as pentraxin 3, is an acute-phase reactant, so serum pentraxin 3 levels may have a significant role in the initiation and development of diabetic retinopathy.

Key words: Diabetes mellitus, diabetic retinopathy, pentraxin-3.

Introduction

Diabetes mellitus (DM) is one of the most common chronic metabolic diseases with many causes in the world. It is characterized by high glucose concentration in the blood. The body's inability causes this to produce insulin or fully use insulin[2]. Diabetes mellitus is associated with microvascular complications, such as neuropathy, nephropathy and retinopathy, induced by chronic hyperglycemia and subsequent hypoxia[3]. Diabetic retinopathy (DR) is a common microvascular complication that is one of the leading causes of adult visual impairment and blindness[4]. The pathophysiology of DR suggests it is highly complex and multifactorial, involving the activation of several interrelated pathways, which all tie into several key mechanisms, namely increased oxidative stress, increased proinflammatory mediators and increased release of growth factors, including vascular endothelial growth factor (VEGF)[1]. Pentraxin 3 (PTX3) is an acute-phase reactant[19]. PTX3 is a 200 amino acid protein that is secreted from the endothelium, macrophages, myeloid cells, dendritic cells, and many other cells in response to cytokines and end toxins such as bacterial products, interleukin-1, and tumor necrosis factor[11]. PTX-3 is one of the endothelium-specific inflammatory cytokines, representing the tissue inflammatory response, especially the one involving the vascular bed, and may reflect the inflammatory status of the vasculature. PTX-3 enhances the procoagulant effect of the endothelial cells and reduces endothelial repair by disabling the effect of the fibroblast growthe factor. It may modulate inflammation-associated tissue damage and offer protection against atherosclerosis (AS). The maximum plasma level of PTX-3 varies depending on the time of the vascular event[5]. PTX-3 is produced in response to ischemic and proinflammatory signals and may directly reflect vascular inflammation 12.

Materials and methods

This case–control study included one hundred and twenty (120) individuals with an age range from 40 to 70 years. Participants were selected from the Diabetic Control Clinic and Diabetes of Specialized Center for Endocrinology and Ibn-Al Haitham Teaching Hospital in Rusafa city in Baghdad from November 2021 to January 2022. Informed consent was taken from each participant. The Scientific Committee of the College of the Medicine/ University of Baghdad approved the study. Individuals were divided into 3 groups: Group 1 included 40 type 2 diabetic patients with retinopathy, group 2 included 40 type 2 diabetic patients without retinopathy and group 3- included 40 persons as controls. Patients with a history of cardiac disease, malig-

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nancies, end-stage renal disease, current or past history of immune-modulating drugs, IV drug users, severe eye disease or retinal detachment, and typ1DM have been excluded from this study. The diagnosis of DM depended on the presence of a history of type2 DM, fasting serum glucose(FSB>126) and Glycated hemoglobin (HbA1 >6.5%) according to WHO criteria. In addition, the diagnosis of DR was made by a senior Ophthalmologist after history taking, clinical examination, and ophthalmological examination. The ophthalmological examination included Fundus examination which was carried out by slit lamp biomicroscope and indirect ophthalmoscopy with volk 90D lens, funds color photograph centered on the macula, and Optical coherence tomography (OCT). Blood involved glycated hemoglobin (HA1C) was measured by autoanalyzer (cobs) C2, and serum lipid profile including total cholesterol, triglycerides, HDL-C, LDL-C and VLDL-C were measured by autoanalyzer (cobs) C3. In addition, serum PTX3 levels were determined by an enzyme-linked immunoassay.

Statistical analysis

Analysis of data was carried out using the available statistical package of SPSS-27 (Statistical Packages for Social Sciences- version 27). Data were presented in simple measures mean, standard deviation, and range (minimum-maximum values). The significance of the difference between different means (quantitative data) was tested using Students-t-test for the difference between two independent means or ANOVA test for the difference between more than two independent means. Statistical significance was considered whenever the P value was equal to or less than 0.05. Correlation and regression were applied for the relationship between two quantitative variables, taking P≤ 0.05 lowest limit of significance.

Results

Significant increase in the mean value of serum pentraxin3 in the diabetic patient with retinopathy as compared to diabetic patients with and without retinopathy as compared to and control (p=0.000) as well as a significant increase in the mean value of serum pentraxin3 in the diabetic patient with retinopathy as compared to diabetic patients without retinopathy (p=0.000) as shown in table 1.

Moreover, a significant increase in the mean value of fasting blood sugar(p=0.0001), HbA1c (p=0.0001), TC (p=0.02), TG (p=0.0001), LDL-C (p=0.03) and VLDL-C (p= 0.0001) in diabetic patients with and without retinopathy as compared to control as demonstrated in table 2.

In addition, a significant positive correlation was found between serum pentraxin3 level and HbA1C in diabetic patients with retinopathy group (r=0.936, p= 0.0001), as shown in figure 1.

Discussion

Inflammation is one potential mechanism of diabetic retinopathy[18]. Hyperglycemia-induced vascular damage is the initial mechanism of retinopathy. Vascular endothelial injury and permeability alteration trigger the inflammatory process[15]. Pentraxin 3 is reported to be a vascular inflammation marker providing prognostic information of vasculopathy[16]. Inflammation is mechanistically involved in the development of DR[14]. PTX3 are acute phase reactants involved in inflammation and endothelial dysfunction. As they are increased in DM, they can be used as prognostic factors for vascular complications such as diabetic retinopathy[17]. Diabetic retinopathy is usually diagnosed too late; therefore, identifying novel biomarkers associated with diabetic retinopathy may facilitate the early detection of individuals at risk and further prevent or reverse diabetic retinopathy. The result of this study revealed higher levels of serum pentraxin3 level in DR patients. This finding was in agreement with previous studies suggesting that increased serum pentraxin 3 concentration may be implicated in the development of DR. This reflects that diabetic retinopathy in T2DM is an inflammatory process associated with increased inflammatory reactants[17,18]. Similar results were done by (20), who suggested that the retinal pigment epithelium and vascular tissues can express PTX3 locally, reflecting that it can be used as a biomarker of vascular inflammation[20]. As well as (10) stated that PTX3 levels are associated with the development and progression of DR in Korean patients with T2DM[10]. This study demonstrated a positive correlation between pentraxin3 plasma concentration and HBA1c in the diabetic retinopathy group in agreement with other recent studies, which reflects that poor glycemic control increases the risk of the development of microvascular complications of DM[21,22].

Conclusions

Higher serum level of pentraxin 3 in diabetic patients with retinopathy and its association with poor glycemic control and pentraxin 3 is an acute-phase reactant, so serum pentraxin 3 levels may have a significant role in the initiation and development of diabetic retinopathy.

Pentraxin 3 (PTX3) (ng/ml)	T2DM Retinopathy	T2DM	Control	P value
	Mean±SD (Range)	Mean±SD (Range)	Mean±SD (Range)	
	4.49±0.79 (3.040-5.690)	2.19±0.40 (1.610-2.970)	0.73±0.23 (0.400-1.260)	0.0001^
	ANOVA	DR x C	DM x C	DR x DM
	0.0001^	0.0001#	0.0001#	0.0001#

Significant^ difference among more than two independent means using ANOVA-test at 0.05 level.

Table 1. Mean value of serum pentraxin3 level in all studied groups.

Parameters	T2DM Retinopathy	T2DM	Control	P value
	Mean ±SD (Range)	Mean ±SD (Range)	Mean ±SD (Range)	
FBS (mg/dL	228.38±64.20 (135-404)	213.68±57.67 (140-320)	88.97±8.25 (68-99)	0.0001^
HbA1C (%)	9.18±1.54 (6.40-12.00)	8.13±1.53 (6.00-11.50)	5.13±0.28 (4.40-5.70)	0.0001^
TC (mg/dL)	194.50±41.10 (127-280)	179.72±43.19 (120-264)	171.65±20.74 (110-192)	0.020^
TG (mg/dL)	221.75±71.23 (153-404)	170.45±43.75 (100-331)	116.73±22.24 (67-148)	0.0001^
HDL-C (mg/dL)	31.93±3.74 (23.0-39.0)	35.83±5.37 (27.0-50.0)	41.08±2.59 (38.0-46.0)	0.0001^
LDL-C (mg/dL)	118.23±37.95 (49.2-190.2)	109.73±41.17 (56.0-195.0)	107.35±19.99 (47.2-133.6)	0.03^
VLDL (mg/dL)	**44.35±14.25 (30.6-80.8)**	**34.09±8.75 (20.0-66.2)**	**23.33±4.47 (13.4-29.6)**	**0.0001^**

Significant^ difference among more than two independent means using ANOVA-test at 0.05 level.

Table 2. Mean value of FBS, HBA1C, TC, TG, HDL-C, LDL-C and VLDL in all studied groups.

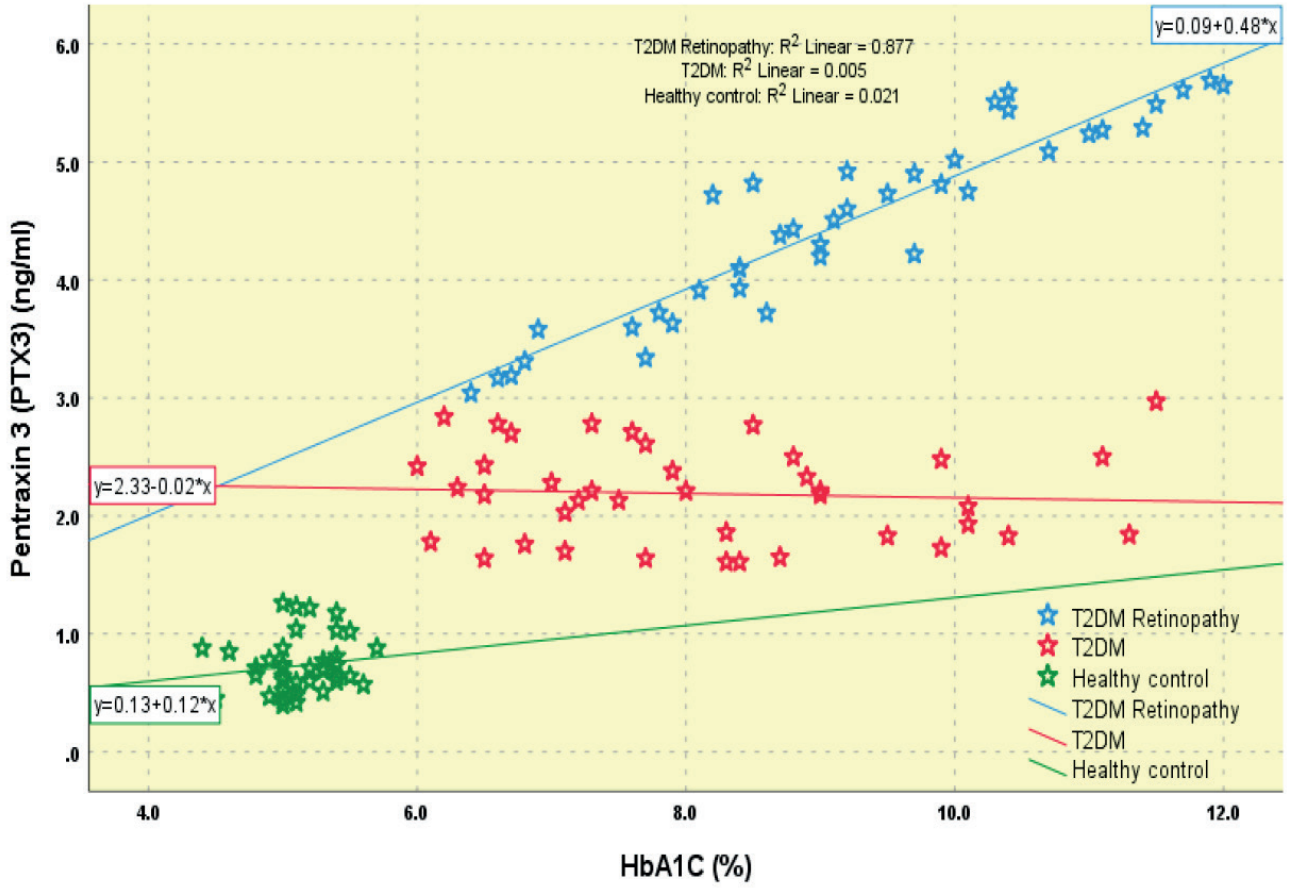

Figure 1. Significant positive correlation between serum pentraxin 3 level and HbA1C in diabetic patient with retinopathy group (r=0.936, p= 0.0001).

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